

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 10

REMARKS/ARGUMENTS

Applicants submitted an Amendment After Final on August 4, 2003, in response to the final Office Action mailed June 4, 2003, in the above-referenced application. The Amendment After Final was not entered by the Examiner. The Advisory Action mailed August 26, 2003, states that new Claim 44 introduced a specific species, e.g., amino acids, and would require further search and consideration.

Applicants note with appreciation the courtesies extended to Applicants' undersigned representative in a telephone interview. As suggested by the Examiner, Applicants are submitting this Second Amendment After Final without new claims 42-44. Applicants also note with appreciation the Examiner's agreement to reconsider the remaining amendments and following remarks.

This is in response to the final Office Action mailed June 4, 2003, in the above-referenced application. Applicants respectfully request entry of the foregoing claim amendments. The amendments do not add new issues for consideration by the Examiner. The amendments merely incorporate subject matter previously considered by the Examiner in dependent claim form into the independent claims. In the alternative, Applicants respectfully request entry of the foregoing claim amendments because the amendments place the claims into better form for appeal.

Dependent claim 29 recites water soluble particles with a coprecipitant having a molecular weight of less than 1,000 Da. Claim 29 is canceled and the subject matter recited therein has been incorporated into each of the pending independent claims. Accordingly the preceding claim amendments do not introduce new matter for consideration by the Examiner because the amendments merely incorporate subject matter from a pending dependent claim into the independent claims. Dependent claims 5 and 10 are amended to correspond to independent claims 1 and 6 from which they depend. Support for this amendment may be found in, for example, claim 29 as filed and in the description on page 6, lines 8- 22 of the application as originally filed.

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 11

The rejections of record are addressed below in the order presented in the final Office Action. Reconsideration and issuance of a notice of allowance by the Examiner is respectfully solicited.

Claims 6-8, 10-12, 22, 24, 25 and 32 are rejected under 35 USC Section 102(b) as anticipated by Randen et al. In addition, Claims 1-12, 20-25, 27, and 32-41 are rejected under 35 USC Section 103 as obvious over Randen et al. Applicants offer the following comments regarding these rejections.

The invention is directed to water soluble particles comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon. The independent claims are amended to incorporate the subject matter of dependent claim 29 and to recite that the coprecipitant has a molecular weight less than 1,000 Da. Applicants respectfully submit that this amendment does not adversely affect the scope of protection available to Applicants, including any protection afforded under the doctrine of equivalents. The amendment merely incorporates subject matter that has been before the Examiner throughout prosecution.

Applicants have discovered that such water soluble particles may be formed by admixing an aqueous solution of a biological macromolecule/coprecipitant with an excess of a water miscible organic solvent. The water soluble particles are formed almost immediately. One technical advantage provided by the invention by the formation of a dehydrated macromolecule is the stabilization of such molecules.

Randen et al. only describe the formation of starch based particles and make no disclosure or suggestion that other materials may be used for the coprecipitation process. The Examiner's attention is directed to column 2 on the front page of Randen et al. and the paragraph under the heading 'Precipitation of Enzymes with Starch' wherein starch with a molecular weight of 12,700 and 100,00 is disclosed. Thus Randen et al. suggest, if anything, that the process described therein is restricted or limited to the use of polymers.

The present invention uses a process of rapid dehydration of biological macromolecules in the presence of a coprecipitate via addition of an aqueous solution to a water miscible solvent. In contrast to Randen et al., the coprecipitate of the claimed invention is a low molecular weight

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 12

compound (i.e., less than 1,000 Da). Accordingly Applicants submit that the claimed invention is novel over Randen et al.

The claimed invention also is nonobvious in view of Randen et al. Polymers such as used by Randen et al. have very different properties as compared to smaller reagents or compounds having a molecular weight of less than 1,000 Da as claimed. One skilled in the art would not expect smaller reagents or compounds (i.e. less than 1,000 Da) would react in a similar fashion to that of a large polymer. Accordingly, there is therefore no motivation from the teaching of Randen et al. for a skilled person in the art to consider the use of smaller particles.

In addition, the milling process referred to in Randen et al. would result in quite different particles than that of the present invention. The Randen et al. milling process would take the coating off the surface, resulting in a particle with no biological macromolecule coating. The milling process will also result in a large distribution of particle sizes. This is in contrast to the present invention, which, as shown in the Figures, results in a small size distribution.

In summary the claimed invention recites coprecipitants of less than 1,000 Da. Randen et al. is directed to a process using polymeric precipitants, as exemplified by the starch with a molecular weight of 12,700 and 100,00. Randen et al. do not teach or suggest the use of small molecular weight coprecipitant as claimed, and there is no motivation to modify the large starch polymer of Randen et al. Further, the Randen et al. milling process would actually remove coating from the surface of the particles. Applicants accordingly submit that the claimed invention is both novel and nonobvious in view of Randen et al. and respectfully request withdrawal of this rejection.

Claim 22 and 32 are rejected under 35 USC Section 103 as unpatentable over Novo WO 97/34919. Applicants offer the following comments.

The Novo publication relates to a method of obtaining protein crystals. The process described in Novo would not result in water soluble particles comprising a coprecipitant core and a dehydrated biological macromolecule coated thereon as recited in the present claims.

Additionally, it is clear from Example 1 that the proteins formed have, at least, a molecular weight of greater than 20 kD. In contrast, the present invention relates to having a coprecipitant less than 1,000 Da as recited in the new claims.

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 13

Novo is directed to a different type of molecule than that claimed. Further, Novo teaches a protein with a high molecular weight, in contrast to the coprecipitant as claimed. Accordingly there is no motivation to modify the method of Novo to provide the claimed invention, and Applicants respectfully request withdrawal of this rejection as well.

Claims 1-5, 13-21, 23, and 26-34 are rejected under 35 USC Section 103 as unpatentable over U.S. Patent No. 5,198,353 to Hawkins et al. and EP 356,239 to Langley et al. Applicants offer the following comments.

Hawkins et al. is directed to a process for preparing a stabilized enzyme dispersion wherein particles are initially produced with protein in a hydrated state. The drying of the particles in Hawkins et al. is only ever carried out in a separate spray-drying step (see Example 5). Thus, a fundamental difference between the present invention and that of Hawkins et al. is that the biological macromolecule in the claimed invention is dehydrated whereas in Hawkins et al. the protein is initially produced in a hydrated state.

The Office points to Column 2 of Hawkins et al. with regard to polymers having a molecular weight from 1,000 Da. However, Hawkins et al. do not teach or suggest here, or elsewhere, using a coprecipitant with a molecular weight of less than 1,000 Da. The Examiner's attention is also directed column 2, line 51, where Hawkins et al. state that "We generally prefer to use molecular weights above 5,000". Additionally, in Table 2 in column 11, it appears that as the molecular weight decreases the biological activity decreases, so that the skilled person would have no motivation to use a coprecipitant less than 1,000 Da.

Further, column 1, line 57, of Hawkins et al. states that a codispersion in water is formed. This is not the same as forming particles. In fact, in view of the dispersion being in water, Applicant submits that even if particles are formed, they cannot be water-soluble.

Langley et al. differs in several respects from the claimed invention as well. Langley et al. is directed to an emulsification process which requires an amphipathic polymeric stabilizer. This stabilizer must be able to interact with both the polymer and the non-polar organic solvent phase. The only polymer exemplified in Langley et al. is the ionic polymer ammonium polyacrylate, which has a molecular weight of 30,000 (see Example 1). Additionally, on column 6, lines 17-18, the polymers are said to have a molecular weight of 4,000 to 300,000.

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 14

Furthermore, the process described in Langley et al. will result in an enzyme distributed throughout a polymer matrix and hence not a coating on the coprecipitant. Langley et al. will therefore not form a coprecipitant core with a dehydrated biological macromolecule coated thereon wherein the coprecipitant has a molecular weight of less than 1,000 Da.

Accordingly, neither Hawkins et al. nor Langley et al., considered singly or together, teach or suggest the claimed invention. Neither teach nor suggest the use of coprecipitants having a molecular weight of less than 1,000 Da. Hawkins et al. produces a hydrated product, not a dehydrated product. Langley et al. produce a product with enzyme distributed throughout a polymer matrix, and not a coating. Thus Applicants respectfully request withdrawal of this rejection as well.

Conclusion

In summary, the cited art does not teach or suggest water soluble particles comprising a coprecipitant core with a dehydrated biological macromolecule coated thereon. Further the cited art does not teach or suggest the use of a coprecipitant with a molecular weight less than 1,000 Da. Accordingly Applicants respectfully submits that the claimed invention is novel and nonobvious and request withdrawal of the rejections of record.

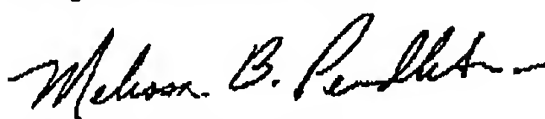
The rejections of record having been addressed above in full, Applicants respectfully submit that the claimed invention is in condition for allowance, which action is respectfully solicited. Should the Examiner have any questions regarding the foregoing, it is respectfully requested that the Examiner contact the undersigned at her convenience.

It is not believed that extensions of time or fees for not addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a) and any fee required

Appl. No.: 10/007,257
Filed: November 13, 2001
Page 15

therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit
Account No. 16-0605.

Respectfully submitted,

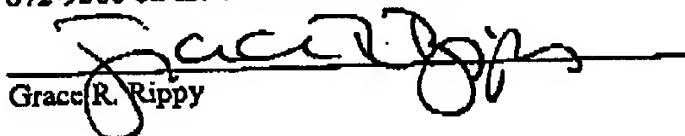


Melissa B. Pendleton
Registration No. 35,459

Customer No. 00826
ALSTON & BIRD LLP
Bank of America Plaza
101 South Tryon Street, Suite 4000
Charlotte, NC 28280-4000
Tel Charlotte Office (704) 444-1000
Fax Charlotte Office (704) 444-1111
CLT01/4621707v1

CERTIFICATION OF FACSIMILE TRANSMISSION

I hereby certify that this paper is being facsimile transmitted to the US Patent and Trademark Office at Fax No. 703-872-9306 on the date shown below.


Grace R. Rippy

December 1, 2001
Date